



Company Overview

NASDAQ: ATHX

www.Athersys.com

October 2019

Forward Looking Statements



NASDAQ: ATHX

This presentation has been prepared by us solely for information purposes. This presentation includes, and our responses to various questions may include, “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the “safe harbor” created by those sections. These forward-looking statements relate to, among other things, the expected timetable for development of our product candidates, our growth strategy and our future financial performance, including our operations, economic performance, financial condition, prospects and other future events. We have attempted to identify forward-looking statements by using such words as “anticipates,” “believes,” “can,” “continue,” “could,” “estimates,” “expects,” “forecasts,” “intends,” “may,” “plans,” “potential,” “should,” “suggest,” “will” or other similar expressions. The forward-looking statements are not historical facts, and are based upon the Company’s current expectations, beliefs, estimates, and projections, and various assumptions, many of which, by their nature, are inherently uncertain and beyond the Company’s control. The Company’s expectations, beliefs and projections are expressed in good faith and the Company believes there is a reasonable basis for them. However, there can be no assurance that management’s expectations, beliefs, estimates, and projections will result or be achieved, and actual results may vary materially from what is expressed in or indicated by the forward-looking statements. Forward-looking statements are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in the forward-looking statements. The Company assumes no obligation to update forward-looking statements to reflect actual results, subsequent events or circumstances or other changes affecting forward-looking information except to the extent required by applicable securities laws.

Information contained in this presentation has been compiled from sources believed to be credible and reliable. However, we cannot guarantee such credibility and reliability. The forecasts and projections of events contained herein are based upon subjective valuations, analyses and personal opinions.

Company Snap Shot (NASDAQ: ATHX)



NASDAQ: ATHX

- ▶ Established international leader in the development of innovative cell therapy and regenerative medicines
- ▶ Multiple clinical programs – **emphasis on critical care indications** with substantial unmet need, high cost of care and quality-of-life burden
- ▶ Lead program, MASTERS-2 registrational Phase 3 trial for Ischemic Stroke enrolling (with Fast Track and RMAT designations) and being conducted under Special Protocol Assessment (SPA) from FDA – accelerated approval pathway in U.S. and Europe
- ▶ Recent positive clinical data from ARDS program (leading to 3rd Fast Track designation)
- ▶ Partnered with HEALIOS K.K. in Japan, enrolling in TREASURE registrational trial for stroke and ONE-BRIDGE trial for ARDS – both leveraging accelerated regulatory path in Japan
- ▶ Robust clinical and preclinical pipeline
- ▶ Solid financial position (\$44.2 million as of June 30, 2019)

Summary Financial Data (Q2, 2019)

Market Cap (as of June 30, 2019)	\$255M
Shares Outstanding	151.8M
\$ Thousands	Six Months ended June 30, 2019
Revenues	\$5,707
Net loss	\$(22,644)
Net cash used in operating activities	\$(16,959)
Net cash provided by financing activities	\$10,537
Cash and cash equivalents	\$44,237

Note: \$44.2 million of cash and cash equivalents as of June 30, 2019

Our Focus: Development of best in class regenerative medicine therapies for areas of substantial unmet medical need

*Neurological, Inflammatory & Immune, Cardiovascular, and Other Indications
with an Emphasis in the Critical Care Segment*



ATHX Regenerative Medicine Pipeline



NASDAQ: ATHX



Experienced Executive Leadership

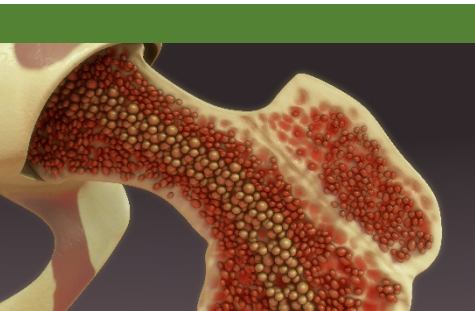


NASDAQ: ATHX

Name	Title	Prior Experience
Gil Van Bokkelen, PhD	Chairman & CEO	
William BJ Lehmann, JD	President & COO	
John Harrington, PhD	CSO Exec. VP, Board member	
Manal Morsy, MD, PhD	Senior VP Global Regulatory Affairs	
Laura Campbell, CPA	Senior VP Finance	
Greg Liposky, MBA	Senior VP Manufacturing	

MultiStem Cell Therapy

Technology & Product Summary:



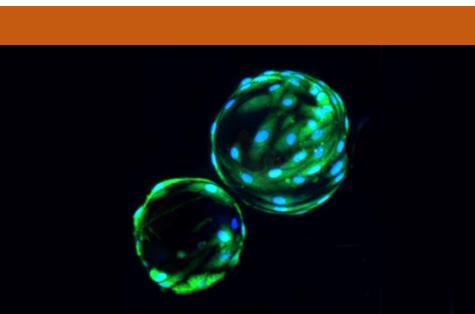
No Ethical Concerns

MultiStem is derived from the bone marrow of healthy adult donors



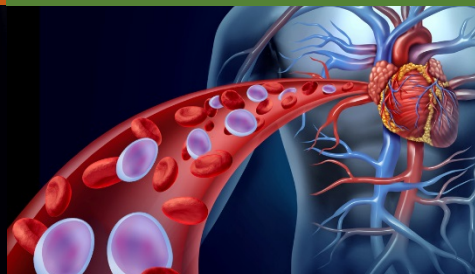
Highly scalable

Millions of doses may be produced from a single donor bank



Based on Proprietary MAPC Technology

Broad IP estate covering core technology, methods of production & areas of use



Promotes Healing and Tissue Repair

Works through multiple mechanisms of action



Given Systemically or Locally

Off the shelf administration with no tissue matching or immune suppression required



Well Characterized Product with Long Shelf Life

> 8 years of stability data on cryogenically stored product

Practical: Simple to Prepare & Easy to Administer



Hospital Pharmacy to Patient in < 1 hour

Enabling Efficient Storage, Access, Product Prep & Inventory Monitoring/Management in the Hospital Environment

SIFU™ Technology



- ❖ Proprietary cryogenic storage system
- ❖ Secure access – inventory is protected at all times
- ❖ Real time informatics on product inventory, storage, system access & usage
- ❖ Enables full “track and trace”... from end to end
- ❖ Simplifies product preparation to a single step after order entry
- ❖ No special facilities or extensive training required

Scalable Manufacturing: Key Competitive Advantage

*Distinctive and Robust Expansion Profile + Integration with Advanced Bioreactor Technology
Enables Unprecedented Commercial Scale*



3D Small Scale
Bioreactors



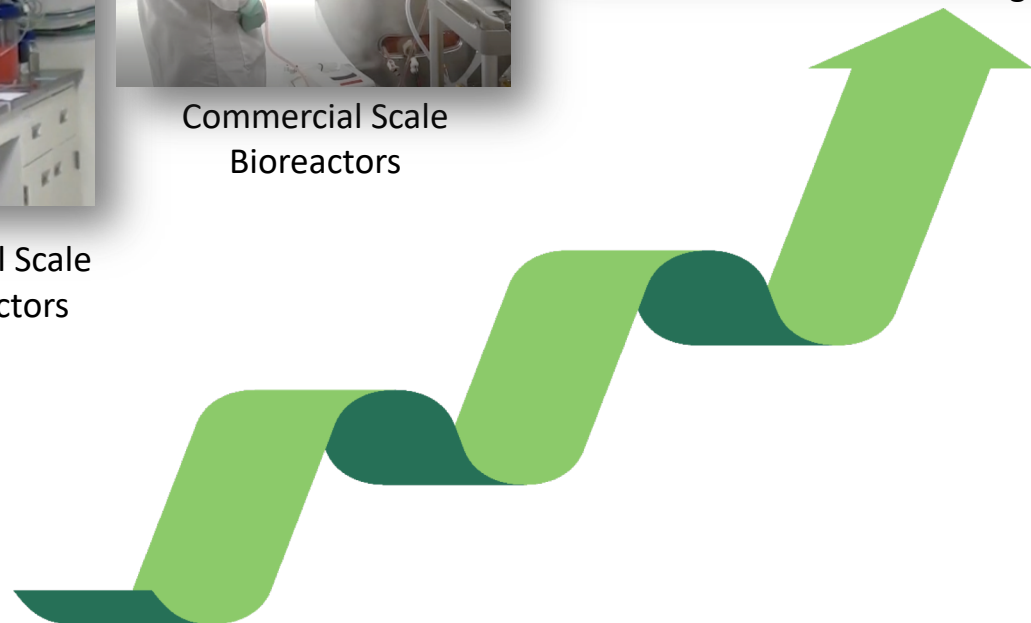
Traditional 2D
Cell Culture



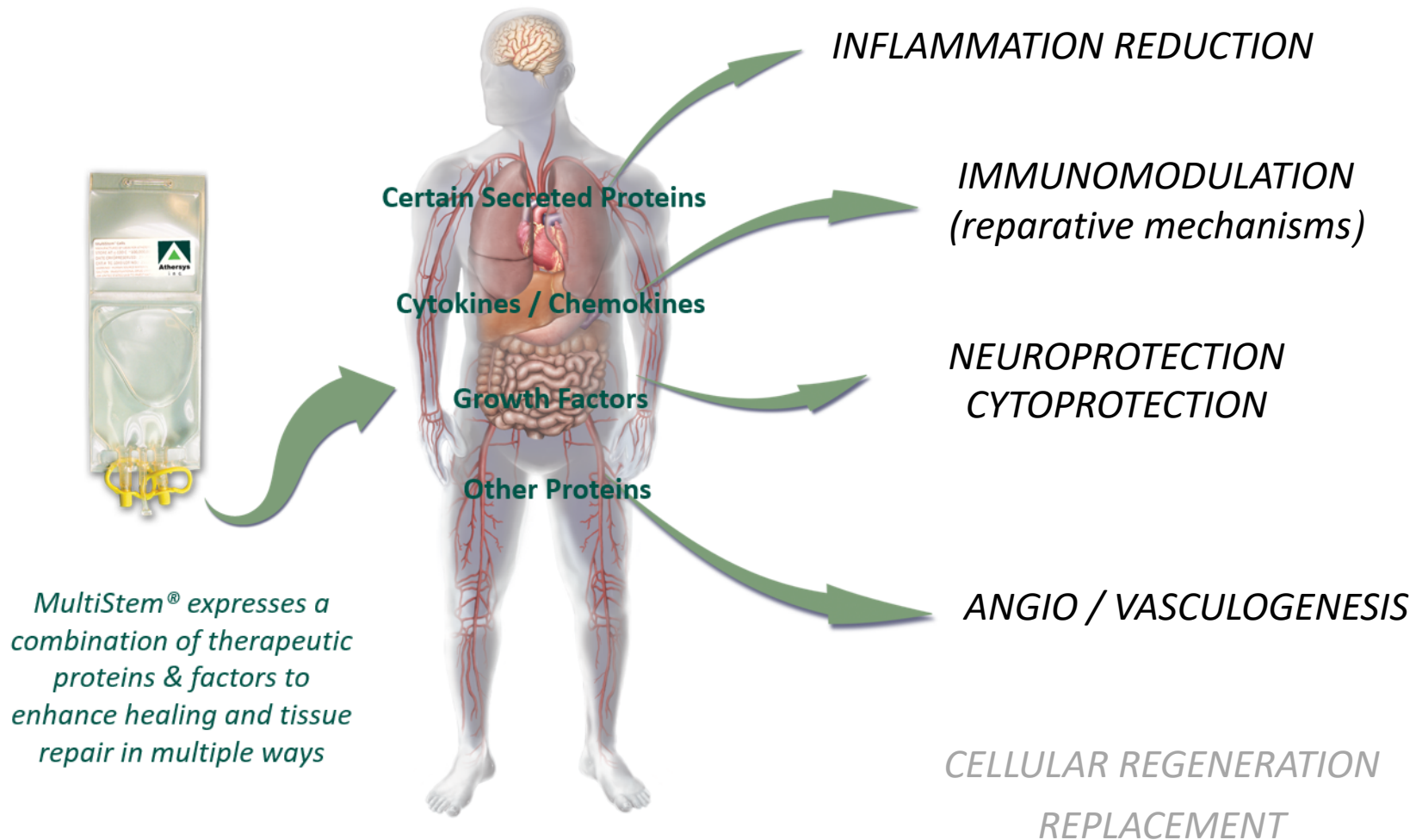
Commercial Scale
Bioreactors



Commercial Manufacturing



Multimodal Biologic Product

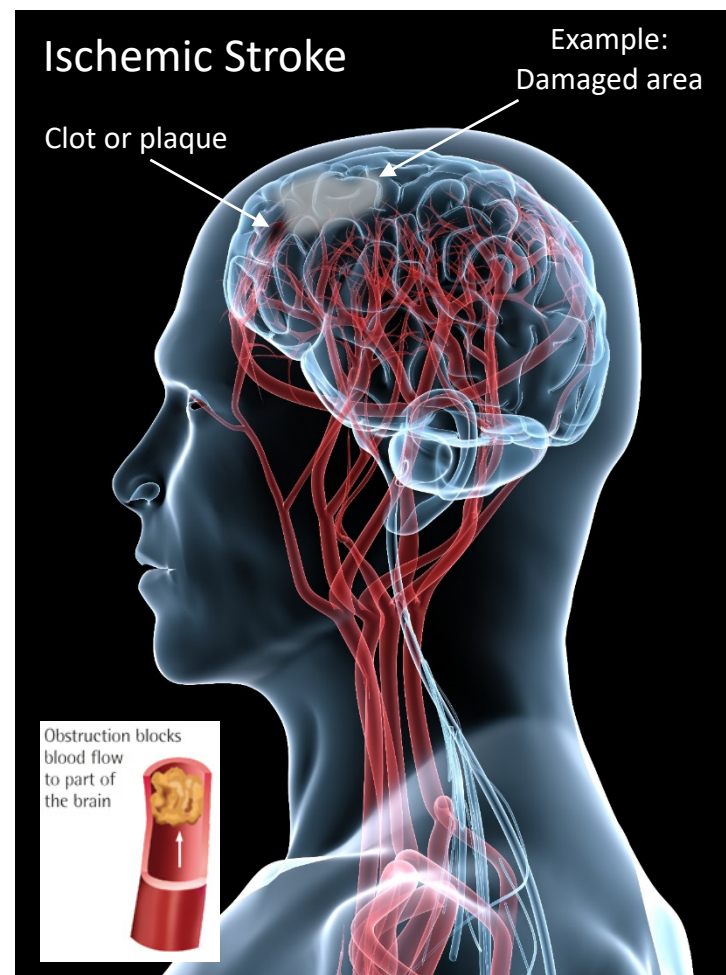


Opportunity for Cell Therapy in Ischemic Stroke

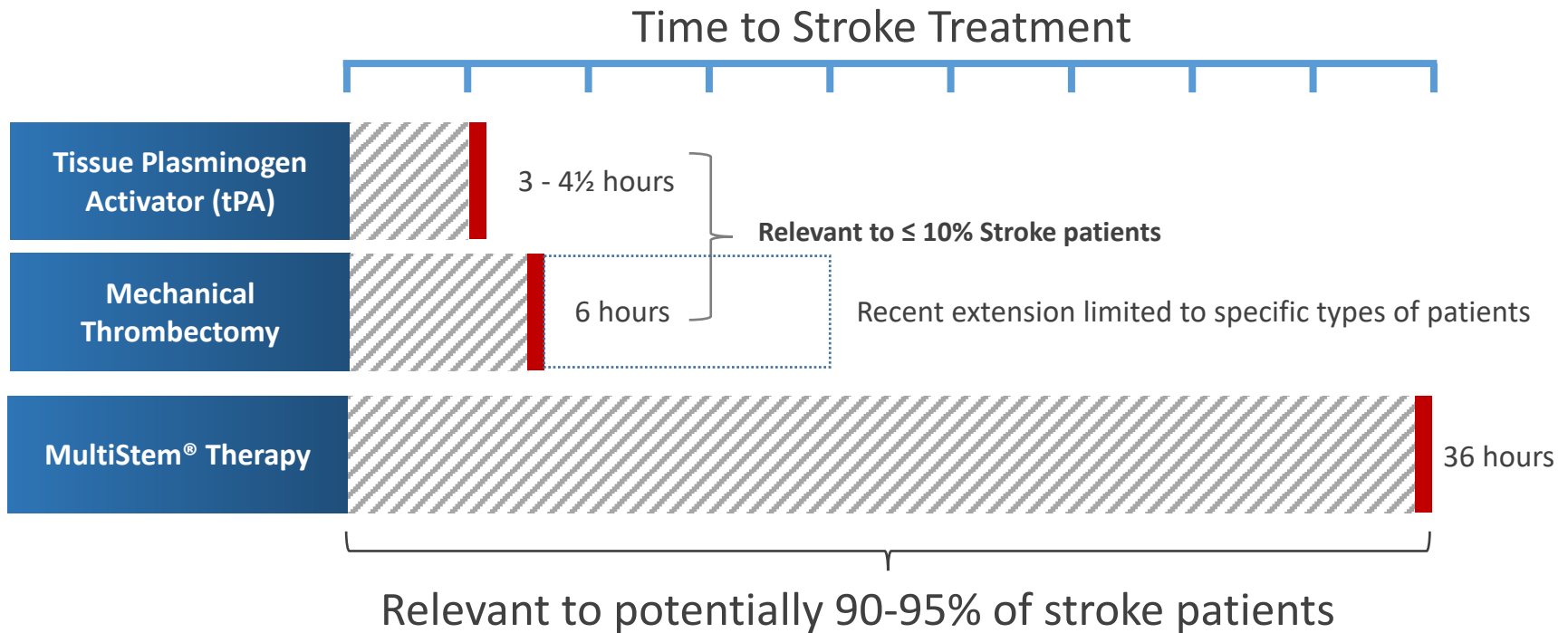
- ▶ **Leading cause of disability** and third leading cause of mortality globally
- ▶ **Annually ~800,000** stroke victims in U.S. **>2.2 Million** (U.S. + EU + Japan), and **~17 Million** globally

Note: >3.4 Million strokes annually in China (including 2.35 Million first time ischemic strokes)

- ▶ **Tremendous unmet need:** tPA must be administered within 3 - 4½ hours of ischemic stroke & MR within 6 – 16 hours
- ▶ With an expanding aging population globally (and increasing obesity in U.S.), the **clinical need and commercial opportunity are expected to increase dramatically in years ahead**



MultiStem Therapy Could Greatly Extend the Treatment Window for Stroke Patients



Spleen's Role in Inflammatory Damage in the Brain following Stroke

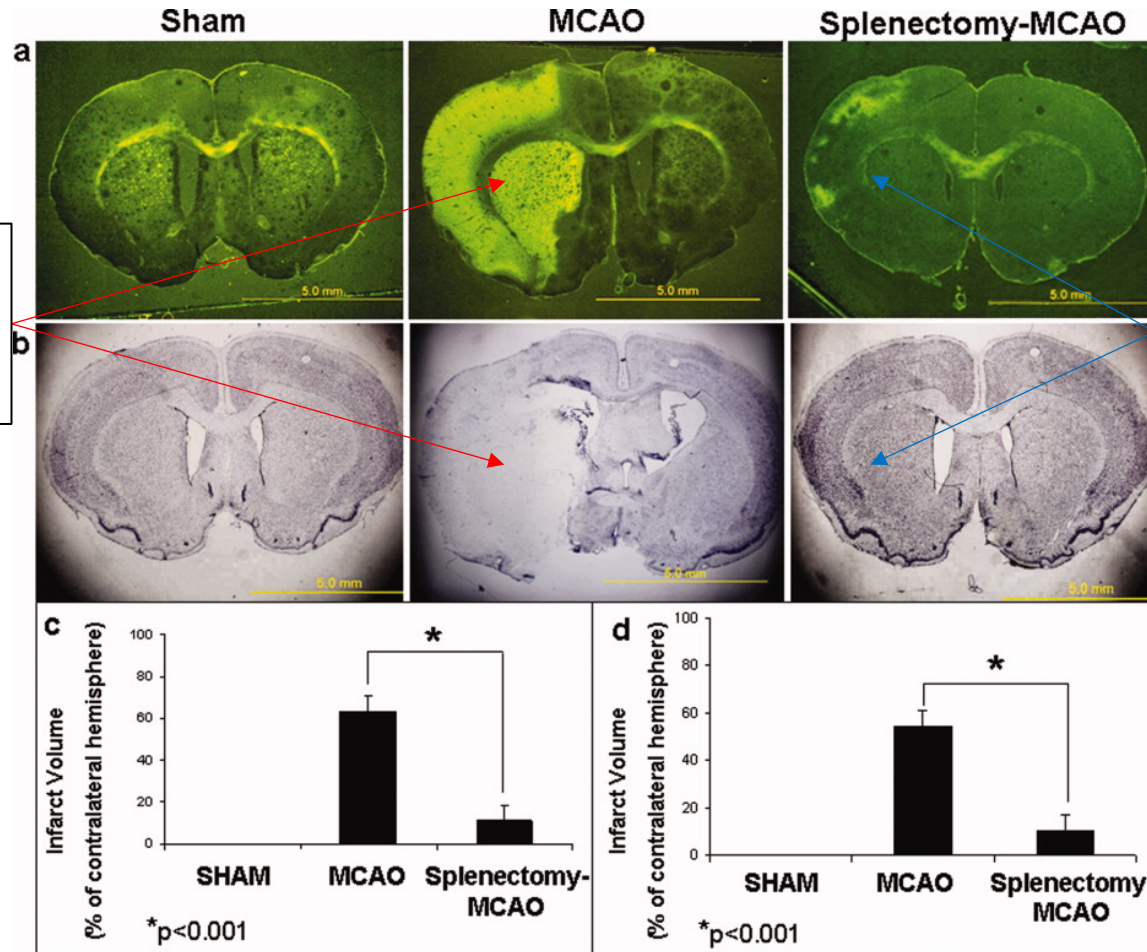
In preclinical models of ischemic stroke, removing the spleen before a surgically induced stroke significantly reduces the inflammatory damage that typically occurs in the brain (but also creates permanent immunological impairment)

Fluoro-Jade Stain

Major loss of brain tissue following MCAO stroke is due to hyperinflammatory response

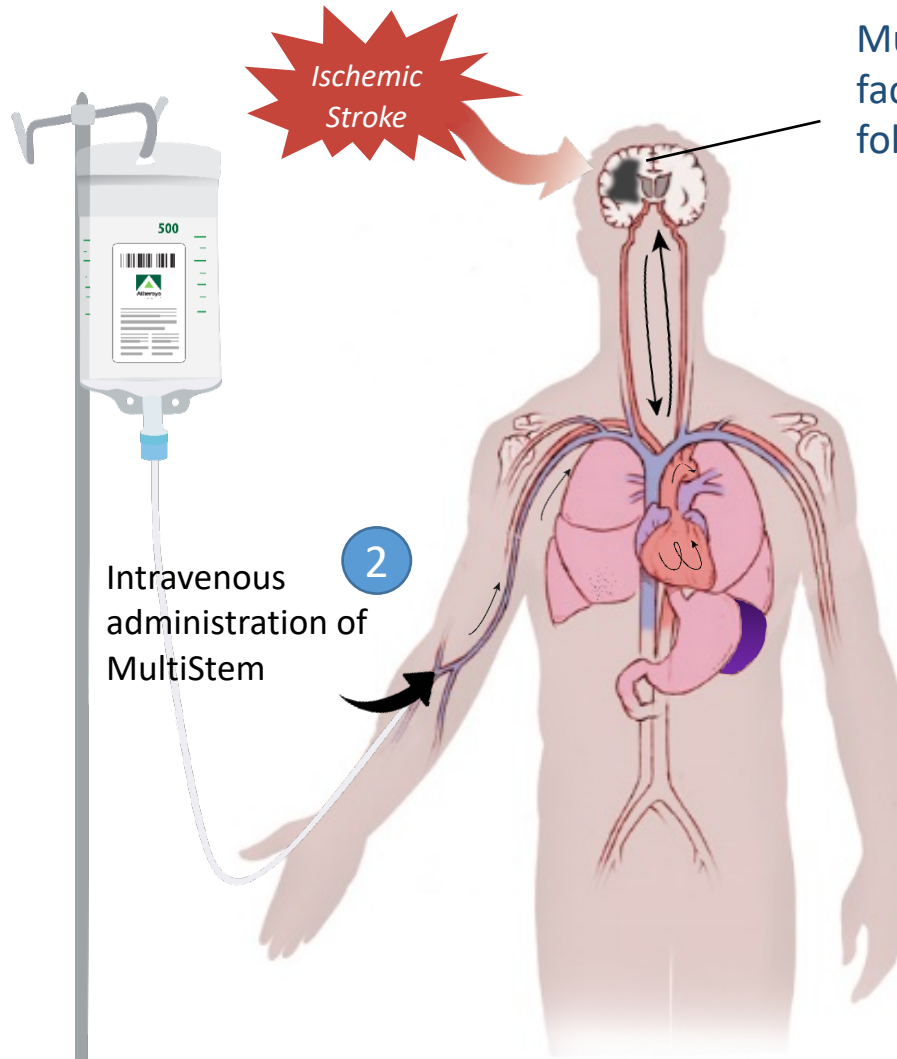
Nissl Stain

Note: MCAO = **M**iddle
Cerebral **A**rtery **O**ccclusion
(i.e. ischemic stroke)



Significantly less neurological damage occurs when spleen is removed prior to stroke

Deep Understanding of Therapeutic MOA's of IV Administration of MultiStem for Stroke



MultiStem works through regulation of multiple factors and pathways important to brain recovery following a stroke.

- 1 Inflammation after stroke leads to greater tissue loss and scarring in the brain. Immune cells coming from the spleen play a major role this response.
- 3 MultiStem cells migrate to the spleen and peripheral immune system and affect key pathways in the brain.
- 4 Simultaneous downregulation of pro-inflammatory processes and upregulation of reparative immune responses promotes recovery.

Representative Publication in *Stem Cells* (2017):
MAPC's Enhance Recovery After Stroke by
Modulating the Immune Response from the Spleen



Contents lists available at ScienceDirect

Experimental Neurology

journal homepage: www.elsevier.com/locate/yexnr

Intravenous multipotent adult progenitor cell therapy for traumatic brain injury: Preserving the blood brain barrier via an interaction with splenocytes

Peter A. Walker^{a,b}, Shinil K. Shah^{a,b,d}, Fernando Jimenez^b, Michael H. Gerber^{a,c}, Hasen Xue^{a,b}, Rochelle Cutrone^e, Jason A. Hamilton^e, Robert W. Mays^e, Robert Deans^e, Shibani Pati^a, Pramod K. Dash^c, Charles S. Cox Jr.^{a,b,d,*}

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Journal of Neurotrauma

Journal of Neurotrauma, Vol. 36, No. 9 | Original Articles

Multipotent Adult Progenitor Cells, but Not Tissue Inhibitor of Matrix Metalloproteinase-3, Increase Tissue Sparing and Reduce Urological Complications following Spinal Cord Injury

Jul, Cynthia R. Gregory, Bradley T. Lang, Hua Xie, Michael J. Fehlings, and Kanton W. Gregory
doi:10.1089/neu.2018.5727

SCIENTIFIC REPORTS

OPEN

Intravenous multipotent adult progenitor cell treatment decreases inflammation leading to functional recovery following spinal cord injury

Received: 14 July 2015
Accepted: 19 October 2015
Published: 19 November 2015

Marc A. DePauli¹, Marc Palmer², Bradley T. Lang^{1,2}, Rochelle Cutrone², Amanda P. Tran², Kathryn M. Madalena², Annelies Bogaerts³, Jason A. Hamilton², Robert J. Deans², Robert W. Mays², Sarah A. Busch^{1,2} & Jerry Silver^{1,2}

Walker et al. *Journal of Neuroinflammation* 2012, 9:228
<http://www.jneuroinflammation.com/content/9/1/228>



JOURNAL OF NEUROINFLAMMATION

RESEARCH

Open Access

Intravenous multipotent adult progenitor cell therapy after traumatic brain injury: modulation of the resident microglia population

Peter A. Walker^{a,b}, Philippa Smith^{a,b}

Stroke



Intravenous Cellular Therapies for Acute Ischemic Stroke

Robert W. Mays, PhD; Sean I. Savitz, MD

The promise of cellular therapies as a treatment for stroke and other injuries and diseases of the central nervous system (CNS) has compelled researchers, clinicians, patients, and the public for the last 2 decades. Various types of cells isolated from numerous tissue sources have demonstrated benefits in improving outcomes in animal stroke models when administered intravenously in an acute time frame (minutes to days) after stroke onset. Data supporting the homing of cells to the brain and proximal to the infarct after intravenous administration is lacking, begging the question "How are cells from an area of distant source, functioning in the injured area?"

exacerbated by matrix metalloproteinases secreted by infiltrating macrophages and neutrophils to further destabilize the blood-brain barrier." Temporal analysis of the accumulation of different inflammatory cells in the brain of stroke-injured animals indicates that microglia/macrophages are activated by 18 hours and most certainly earlier, and peak by 48 hours after stroke, remaining abundant for as long as 96 hours. Neutrophils peak at 48 hours remaining elevated at 96 hours, whereas T lymphocytes appear later in the process (72–96 hours). These data highlight the intricate but robust response of the neuroinflammatory system after initiation of the stroke.

A Hamilton

Bedi et al. *Journal of Neuroinflammation* (2018) 15:84
<https://doi.org/10.1186/s12974-018-1122-8>

Journal of Neuroinflammation

RESEARCH

Open Access

Therapeutic time window of multipotent adult progenitor therapy after traumatic brain injury

Supinder S. Bedi^{1*}, Benjamin M. Aertker¹, George P. Liao¹, Henry W. Caplan¹, Deepa Bhattarai¹, Fanni Mandy¹, Franciska Mandy¹, Luis G. Fernandez¹, Pamela Zelnick¹, Matthew B. Mitchell¹, Walter Schiffer¹, Margaret Johnson¹, Emma Denson¹, Karthik Prabhakara¹, Hasen Xue¹, Philippa Smith¹, Karen Uray¹, Scott D. Olson¹, Robert W. Mays¹ and Charles S. Cox Jr.^{1,2,3}



REGENERATIVE MEDICINE

Multipotent Adult Progenitor Cells Enhance Recovery After Stroke by Modulating the Immune Response from the Spleen

BING YANG^{1,2*}, JASON A. HAMILTON^{1,2}, KRISTAL S. VALENZUELA¹, ANNELIES BOGAERTS¹, XIAOPEI XU¹, JAROSLAW ARONOWSKI¹, ROBERT W. MAYS¹, SEAN I. SAVITZ²

Key Words: Rat model • Adult human bone marrow • Bone marrow stromal cells • Cellular therapy

944 • The Journal of Neuroscience, January 19, 2011 • 31(3):944–953

Development/Plasticity/Repair

Multipotent Adult Progenitor Cells Prevent Macrophage-Mediated Axonal Dieback and Promote Regrowth after Spinal Cord Injury

Sarah A. Busch,¹ Jason A. Hamilton,² Kevin P. Horn,¹ Fernando X. Cuascat,¹ Rochelle Cutrone,² Nicholas Lehman,² Robert J. Deans,² Anthony E. Ting,² Robert W. Mays,² and Jerry Silver¹

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Behavioural Brain Research

Volume 362, 19 April 2019, Pages 77–81

Research report

Systemic multipotent adult progenitor cells improve long-term neurodevelopmental outcomes after preterm hypoxic-ischemic encephalopathy

Melinda Barkhuizen^{a,b,c,1}, Ralph van Mechelen^{a,b}, Marjine Vermeer^{a,b}, Peter Chedraui^{a,b}, Dean Paes^b, Daniel L.A. van den Hove^{b,f}, Bart Vaes^g, Robert W. Mays^g, Harry W.M. Steinbusch^h, Nicola J. Robertson^b, Boris W. Kramer^{a,b,h,i}, Antonio W.D. Gavilanes^{a,b,d,i,j,k}

MultiStem Stroke Clinical Trial

Results from MASTERS-1 (Phase 2)

MultiStem Administration for Stroke Treatment and Enhanced Recovery Study

Established & Well Accepted Regulatory Endpoints for Ischemic Stroke



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



There are currently 2 well accepted regulatory endpoints for therapies being evaluated for efficacy in treating acute ischemic stroke:

► **Excellent Outcome**

- Proportion of patients that achieve an excellent score in each of three established clinical rating scales: NIHSS, Barthel Index, Modified Rankin Scale
- This essentially represents the proportion of patients that achieve full recovery over clinical assessment period

► **mRS Shift Analysis**

- Reflects improvement across the entire disability spectrum during the clinical evaluation period
- Note: PMDA expressed a slight preference for Excellent Outcome, whereas FDA and EMA expressed a slight preference for mRS shift analysis as primary assessments (each w/ the alternative endpoint as main secondary assessment)

A map of the United States with state boundaries outlined in black. Twenty orange dots are placed on the map to indicate sampling locations. The dots are distributed across the country, with a higher concentration in the eastern half, particularly in the Northeast and Southeast. There are also dots in the West, the central US, and Alaska.



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MultiStem Clinical Study in Ischemic Stroke: MASTERS-1 (B01-02)



NASDAQ: ATHX

Trial Design Overview

- IV administration of MultiStem or placebo 24-36 hours post onset of ischemic stroke
 - Double-blind, placebo-controlled
 - Dose escalation phase, followed by efficacy phase
 - Dose of 1.2 billion cells
 - Cortical cerebral ischemic stroke
 - 12-month final endpoint (including MRI)
- Safety evaluated
 - Adverse events, infusion reactions, infections, mortality
- Multiple clinical scales used to evaluate efficacy:
 - modified Rankin Scale (**mRS**) = Global disability
 - NIH Stroke Scale (**NIHSS**) = Neurological and motor skill deficits
 - Barthel Index (**BI**) = Ability to engage in activities of daily living (e.g., walking, dressing, feeding, toiletry, bathing)
- Exploratory endpoints evaluating MOA and clinical impact
 - Biomarkers (circulating immune cells and serum cytokine levels)
 - Hospitalization

Key Eligibility Criteria – Original Design

Cortical Stroke
NIHSS 8-20 at baseline (24 hours), stable deficit
Administration within 24-36 hours
tPA or device patients eligible if other criteria met

Key Changes to Accelerate Enrollment

Cortical Stroke
Administration window extended to 48 hours • Earlier treatment better. However, local cell processing limitations (e.g., open limited hours Monday through Friday) constrained enrollment
Included patients receiving <u>both</u> tPA-MR • Background rates/expectations for this group not well known • However, several of our sites treating patients receiving both tPA and mechanical reperfusion (MR), and such patients seemed to meet criteria

Selected Baseline Demographics Information

Patient sample	MultiStem n=65	Placebo n=61
Age, mean, range	61.8 41-83	62.6 37-80
Sex, male	53.8%	54.1%
NIHSS, mean, median	13.4 13.0	13.3 13.0
MRI DWI Lesion size, mL, mean, median	51.6 42.3	54.8 41.1
Administered		
iv tPA	44.6%	47.5%
iv tPA+device	12.3%	14.8%

Final Trial Results: Treatment w/ MultiStem Shows Significant Benefit at One Year



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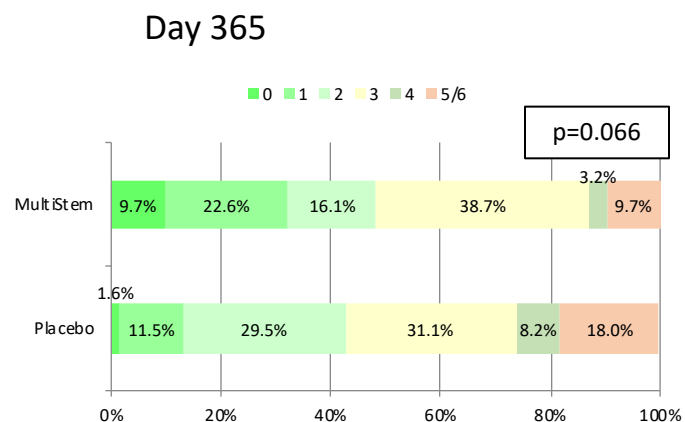
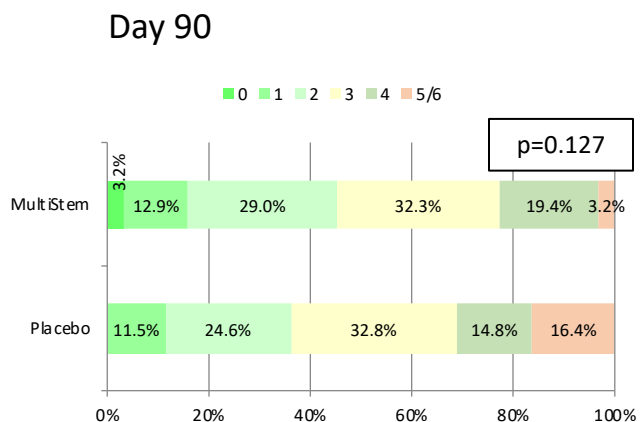
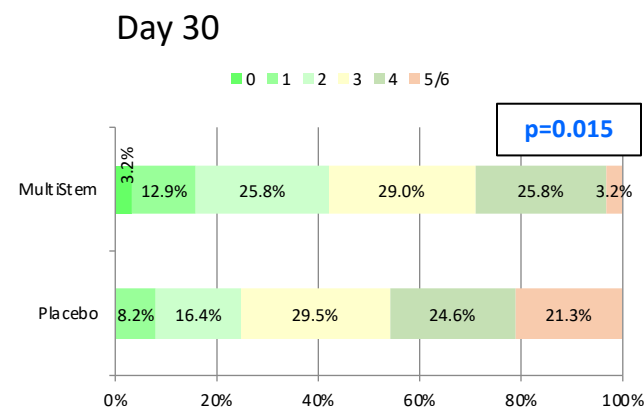
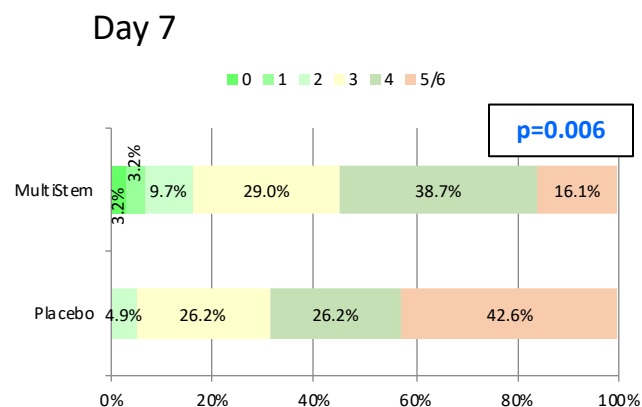
*Proportion of Subjects Achieving Excellent Outcome Increases Over Time
(Patients Achieving NIHSS 0 or 1 and mRS 0 or 1, and Barthel Index ≥ 95)*

		Day 90	Δ at Day 90	Day 365	Δ at Day 365
ITT (All Trial Subjects):	MultiStem (n=65) Placebo (n=61)	15.4% vs. 6.6%	8.8%	23.1% vs. 8.2%	14.9% p = 0.02
Early MultiStem Treatment (≤ 36 Hrs) vs All Placebo	MultiStem (n=31) Placebo (n=61)	16.1% vs. 6.6%	9.5%	29.0% vs. 8.2%	20.8% p < 0.01
Original Trial Protocol: Early MultiStem Treatment (≤ 36 hrs) vs Placebo*	MultiStem (n=27) Placebo (n=52)	18.5% vs. 3.8%	14.7%	29.6% vs. 5.8%	23.8% p < 0.01

* As specified in original trial design, analysis includes patients that received either no reperfusion therapy, non-responder tPA or mechanical reperfusion (MR) patients in addition to investigational product (i.e. excludes a limited number of subjects receiving both tPA and MR)

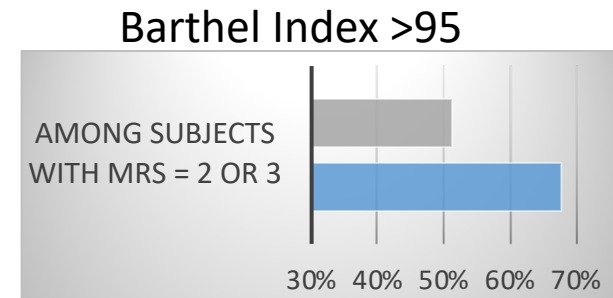
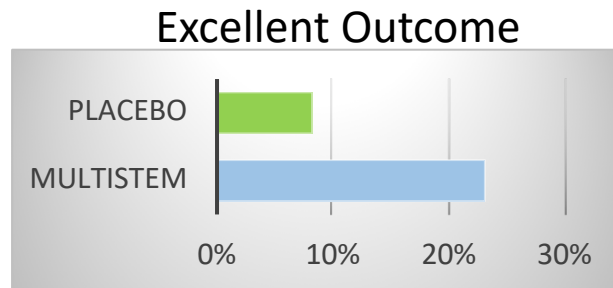
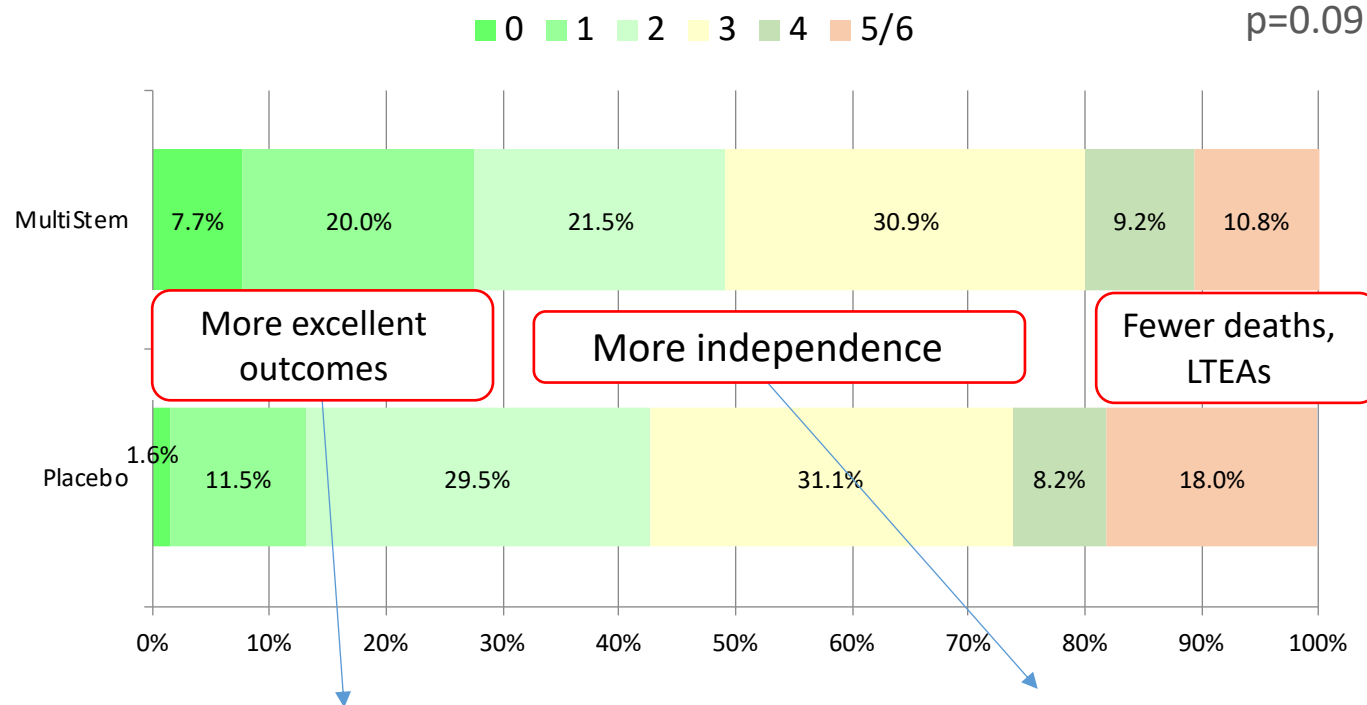
MultiStem Improvement Evident Across the Severity Spectrum – Early-Treated MultiStem Subjects v. Placebo

mRS Shift Analysis



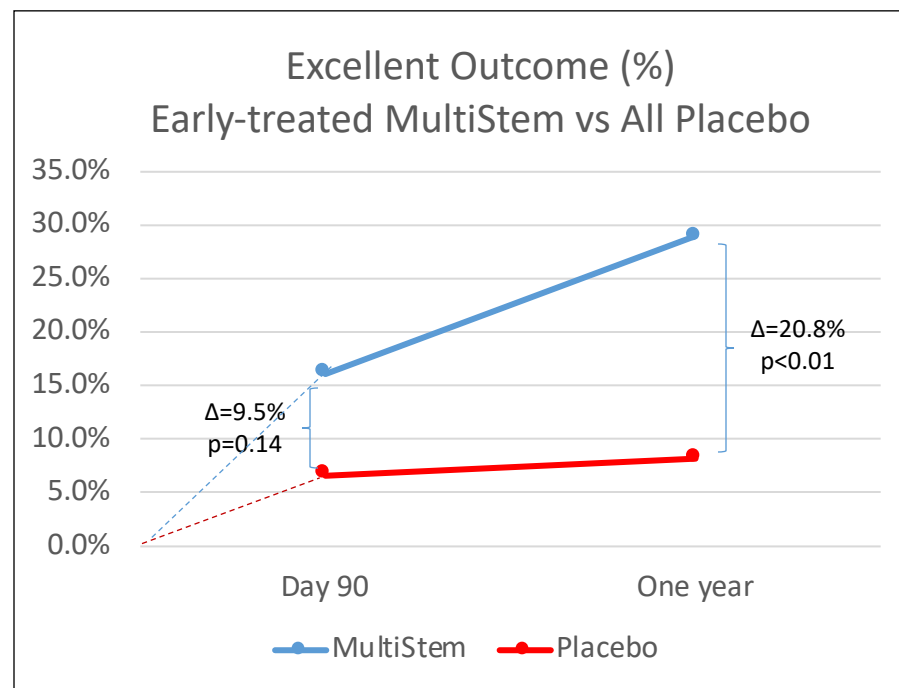
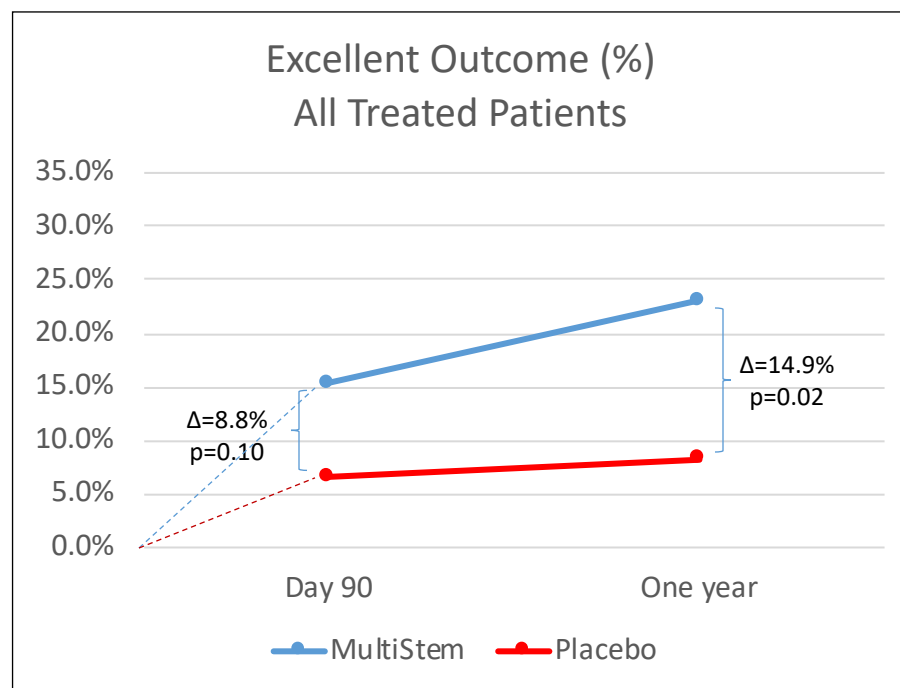
Note: Early-treated means <36-hour administration, representing 31 MultiStem subjects

mRS Distribution (Shift) at One Year – ITT



Improvement in Excellent Outcome Following Treatment with MultiStem Therapy

In contrast to longstanding clinical experience, MultiStem treated patients exhibit meaningful improvement beyond the initial 90-day recovery period



Excellent Outcome = mRS ≤1, NIHSS ≤1, and BI ≥95

Note: Early-treated means <36-hour administration, representing 31 MultiStem subjects

Other Findings from MASTERS-1 Study

- ▶ **Safety: Intravenous MultiStem well tolerated by Stroke patients**
 - No infusional or allergic reactions, and no abnormal patterns in safety labs or vital signs
 - Adverse events consistent with expectations and experience for stroke patients of this type
- ▶ **Administration of MultiStem within 36 hours associated with meaningfully better outcomes for patients, including:**
 - Substantially higher proportion of patients achieving excellent score in Barthel Index (activities of daily living), 67.7% (MultiStem treated) vs 44.3% (Placebo), $p = 0.03$
 - Meaningful reductions in ICU time and initial hospitalization
- ▶ **Reduction in serious complications following Stroke**
 - Reduction in life threatening AEs and death
 - Reduced incidence of secondary infections
- ▶ **Benefits observed across treated population, e.g., age, stroke severity, reperfusion vs. no reperfusion therapy**

Additional Clinical Observations from the MASTERS-1 Stroke Study

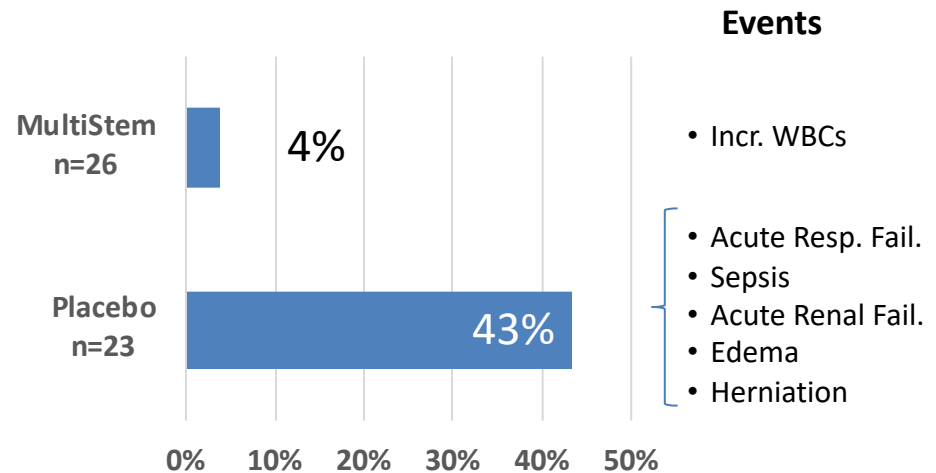
Among the most severely disabled stroke patients, a substantial reduction observed in serious and life-threatening adverse events



In the aftermath of a severe stroke, patients are highly susceptible to a range of severe and potentially life-threatening complications

Severe Stroke (NIHSS 15+) Subjects

% Subjects with Grade 3-5 Adverse Events Through Day 30



Clinical Biomarker Data: MultiStem has an Impact on Key Inflammatory Markers

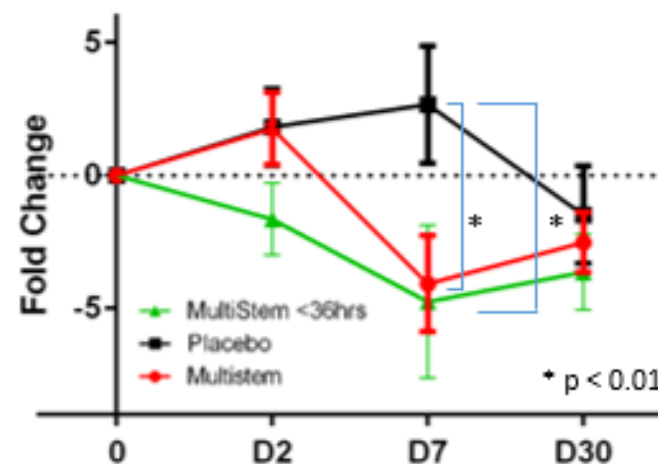
Circulating CD3+ T-cell Levels, Safety / ITT Population

	MultiStem	Placebo
Day 0	18.5%	18.8%
Day 2	18.4%	23.3%
Change	(0.1%)	4.5%
	P=0.001	

Note: Evaluates available data from ITT population; for cytokine analyses, controlling for differences in baseline values and outliers

Impact on key biomarkers (circulating immune cells and key inflammatory cytokines), provides direct support for therapeutic rationale and MOA's.

Fold Change for Key Inflammatory Cytokines (Aggregated), Safety / ITT Population



Cytokine	Day 7, p-value
IL-1 β	0.01
TNF α	0.03
IL-6	0.03
IL-12	0.12
INF γ	0.03
IL-2	0.11

HEALIOS K.K. Partnership Overview

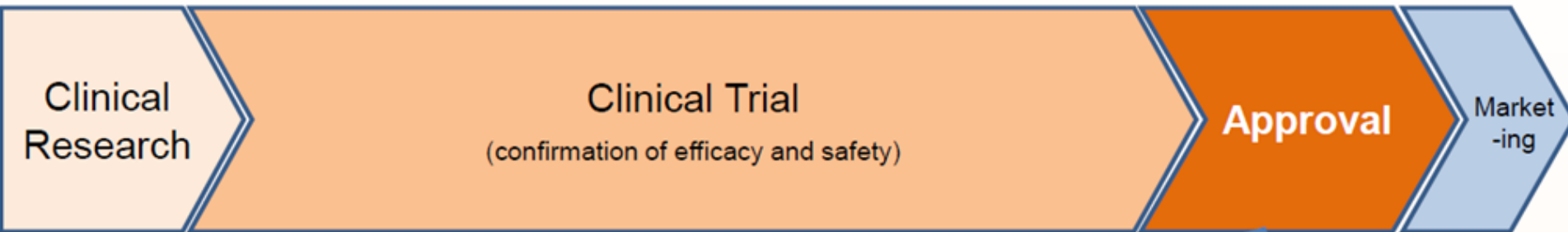
- ▶ Initial partnership with Healios established January 2016
 - **\$15 million up front** payment with **> \$225 million total additional potential payments**, subject to certain credits, **plus tiered double-digit royalties**
- ▶ Initial therapeutic focus: Ischemic stroke = most prevalent cardiovascular disease in Japan (leading cause of serious disability)
 - High proportional incidence
 - Rapidly expanding population of elderly (i.e. most susceptible)
- ▶ Well-positioned for accelerated approval under new regulatory framework
 - Rapid approval possible based on a single trial
 - March 2017 = Priority Review designation granted to Healios under *Sakigake*
 - Trial initiated and first patient enrolled in November 2017
 - High degree of clinical investigator enthusiasm
- ▶ Once approved, clear and efficient reimbursement pathway
 - Highly centralized with a defined, efficient process (single point of entry)
 - Reimbursement applies universally to all payer groups in Japan
 - Attractive price point possible (e.g. based on recent precedents for Regenerative Medicine products)



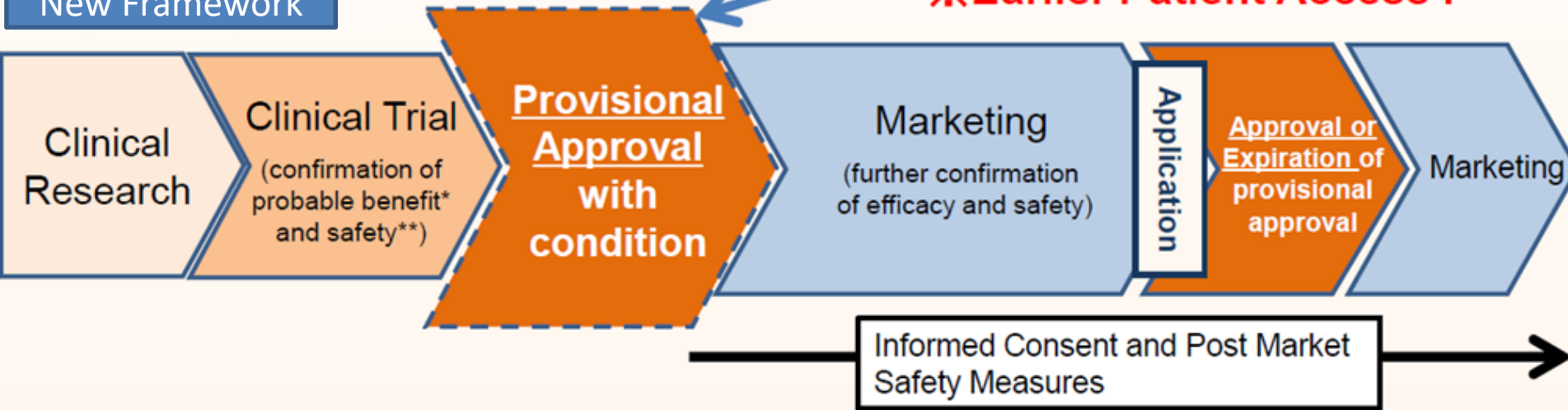
Recently Implemented Accelerated Approval System for Commercialization of Cell Therapy Products in Japan



Traditional Approach



New Framework



* Probable benefit: Confirmation of efficacy with small patient population.
** Safety: Earlier detection and evaluation of adverse events.

Expanded Collaboration – Announced June, 2018

- ▶ Healios obtains expanded exclusive license to certain programs in Japan and globally
 - Under terms of the collaboration expansion, Healios obtained development and commercialization rights to include treatment of ARDS and certain transplantation indications in Japan, plus defined Ophthalmological indications and rights to Organ Bud based treatments globally (for \$20 million license fee)

- ▶ Economic impact for ATHX = **\$43.1 million** (plus up to **~\$360 million** in additional potential milestone payments, subject to certain credits, plus tiered double-digit royalties)
 - **Initial equity investment of \$21.1 million** completed in March 2018 (at premium) in exchange for an initial 8.7% equity stake
 - **Plus \$20 million in license fees** - for license expansion
 - Healios also obtains ability to acquire up to 4 million shares in ATHX (via warrant)
 - Warrants priced at premium to recent market price (minimum of \$1.76 per share)

MASTERS-2: Pivotal Phase 3 Study in Ischemic Stroke

(Authorized by FDA under **SPA**, w/ **Fast Track** and **RMAT** designations)



NASDAQ: ATHX

Trial Overview – (focused on North America and Europe – initiated and enrolling subjects)

- ▶ Intravenous administration of investigation product (MultiStem cell therapy or placebo) within **18 - 36** hours post onset of ischemic stroke...Note: may be administered on top of standard of care for eligible patients
 - **300 subjects**
 - Double Blind, randomized, placebo-controlled study
 - 1:1 ratio (MultiStem [n=150] or placebo [n=150])
 - Same dosing profile for MASTERS-1 (1.2 B cells, administered IV)
 - NIHSS 8 – 20 at baseline
 - Cortical cerebral infarct
 - IV tPA, mechanical thrombectomy or both treatments (for limited number of subjects) allowed if patient not showing substantial improvement
 - 90-day primary clinical assessment, 12-month double blind follow-up (e.g. secondary endpoints)
- ▶ Evaluating safety
 - Mortality, adverse events, infections, infusion reactions
- ▶ **Primary efficacy endpoint** = mRS score at Day 90 evaluated by shift analysis
- ▶ **Key secondary efficacy** variables include differences between MultiStem and placebo treatments with respect to the following:
 - Proportion of subjects achieving an Excellent Outcome (mRS ≤ 1 , NIHSS ≤ 1 and Barthel Index ≥ 95) at day 365
 - Proportion of subjects achieving an Excellent Outcome (mRS ≤ 1 , NIHSS ≤ 1 and Barthel Index ≥ 95) at day 90
 - Proportion of subjects with mRS score of ≤ 2 at Day 90

Note: Bolded indicate changes from Phase 2 B01-02 trial design.



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Other Portfolio Programs

Acute Pulmonary Medicine

- ▶ Acute Respiratory Distress Syndrome (ARDS) afflicts approximately 400,000 to 500,000 patients in Europe, the United States and Japan annually, and >670,000 patients in China
 - ARDS represents a major area of unmet medical need, with a high rate of mortality and high level of morbidity, and typically requires extended intensive care hospitalization (e.g. ICU)
 - Very high cost of care and QOL impact → **Another potential multibillion \$ market opportunity**
- ▶ MultiStem conveys benefit through multiple mechanisms relevant to acute pulmonary inflammatory damage
 - Published data illustrates impact on reducing inflammatory damage in pulmonary system
 - Upregulation of reparative cell types and pathways
- ▶ Athersys and collaborators evaluating potential of MultiStem in ARDS → Positive results from exploratory clinical trial announced January 2019
 - Fast Track designation from FDA announced May 14th, 2019
 - Presentation at American Thoracic Society meeting May 20th, 2019
- ▶ **New:** Healios obtained PMDA authorization of CTN and has commenced trial in Japan; Announced first patient was enrolled in April 2019



MultiStem Reduces Inflammation in Human Lungs with Ischemic Reperfusion Injury

Assessment of human lungs isolated from organ donors that exhibit significant inflammation prior to use in transplantation, perfused with MultiStem or vehicle (saline).

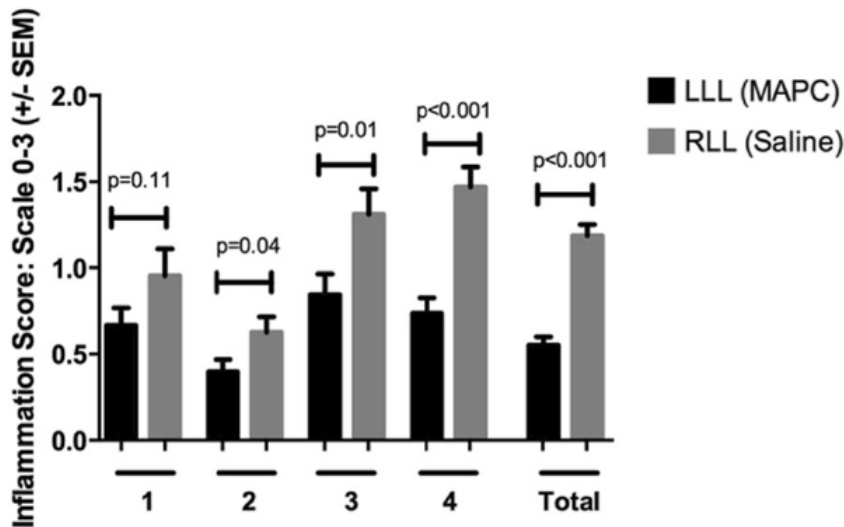


Figure 3 Semi-quantitative scoring demonstrates significant decrease in overall inflammation in the MAPC-treated LLL compared to the vehicle-treated RLL in three out of four lungs and in aggregate. Means $\pm$ SD of pooled observations from three blinded observers are depicted.

Note: Organ donor lungs originally designated for use in transplantation, but were disqualified due to pulmonary inflammation that occurs after harvest, resulting in poor pulmonary function.

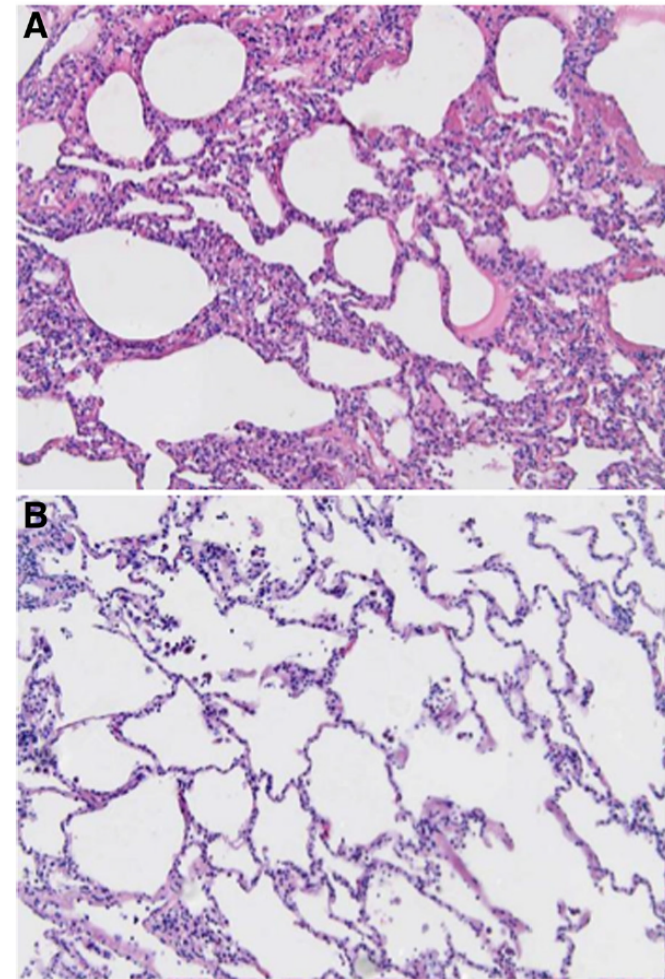


Figure 4 Representative photomicrographs from lung 1 demonstrate (A) alveolar septal thickening, edema, and perivascular and peri-bronchial inflammatory cell infiltrates in the control-treated RLL vs (B) minimal to no significant inflammation in MAPC-treated LLL. Original Mag 200 $\times$.

ARDS Trial – Initial Results

(Presented at ATS – May 20, 2019)

Exploratory Ph. 2 MUST-ARDS Trial: Randomized, double-blind, placebo-controlled trial evaluating patients through 28-day clinical assessment (standard) with one year follow up.

All Subjects	MultiStem	Placebo
Number	20	10
Ventilator-free days (mean)	12.9	9.2
(median)	18.5	6.5
ICU-free days (mean)	10.3	8.1
(median)	12.5	4.5
Mortality (d28)	25%	40%
Patients w/ Low pulmonary function: PaO ₂ /FiO ₂ < 150 mm at baseline	MultiStem	Placebo
Number	8	8
Ventilator-free days (mean)	14.6	8.0
(median)	18.5	3.5
ICU-free days (mean)	11.4	5.9
(median)	12.5	1
Mortality (d28)	25%	50%

The Healios ONE-BRIDGE study is evaluating pneumonia-induced ARDS



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Post-hoc analysis of Pneumonia-Induced ARDS (Severe cases – $\text{PaO}_2/\text{FiO}_2$ Ratios at Day 0, Pre-infusion < 150)

	MultiStem	Placebo
Day-28 Mortality	20%	50%
Ventilator-free days	14.8	7.5
ICU-free days	12.0	5.0

Data for severe cases of pneumonia-induced ARDS shows an even greater difference in mortality rate, Vent free and ICU free days between the subjects treated with MultiStem and the patients in the placebo-controlled group.

Other Neurological Injury & Disease Areas of Interest

IV Administration of MultiStem to Promote & Accelerate Healing & Repair

Work conducted in preclinical models – with multiple publications in leading scientific journals

❖ **Ischemic Stroke**

Supported by StrokeMAP

❖ **Traumatic Brain Injury (TBI)**

Supported by NIH

❖ **Neonatal Hypoxic Ischemia**

Supported by NIH

❖ **Spinal Cord Injury**

Supported by Third Frontier

**Acute
Neurological
Injury**

❖ **Multiple Sclerosis**

Supported by Fast Forward, MS Society

❖ **Parkinson's Disease**

Supported by Michael J. Fox Foundation

**Chronic
CNS Disease**



Also: Orphan status granted by FDA for MPS-1 (Hurler's Syndrome)

Opportunity in Trauma

- ▶ Trauma is the leading cause of death and serious disability among individuals age <45 in the U.S.
 - Leading cause of life years lost among individuals up to age 75... and third leading cause of death overall
 - Significant impact on youth, elderly and military personnel (battlefield trauma & VA patients)
 - Huge economic and quality of life impact
- ▶ ATHX team and independent collaborators have worked extensively in several areas of trauma (numerous publications)
 - Traumatic Brain Injury (TBI)
 - Spinal Cord injury
 - ARDS (e.g. precipitated by trauma)

} Critical Care Segment
- ▶ Mechanistically the hyperinflammatory response following trauma is the same as for stroke, w/ similar effects
 - Emanates from the spleen & peripheral immune system, causing secondary damage
 - Response frequently results in immunodepression – with patients susceptible to a range of complications that inhibit or complicate recovery
- ▶ ATHX collaborating with leading Tier 1 Trauma Center in U.S. with funding provided by MTEC (Department of Defense) and UTH for planned Phase 2 trial (~150 patients – double-blind randomized, placebo-controlled)

► Multiple important objectives achieved recently

- **Sakigake priority review designation** for ischemic stroke program in Japan (obtained by Healios with our support)
- **Healios initiation of TREASURE trial**
- **Fast Track and RMAT designations** granted by FDA for our Phase 3 Stroke program
- **Positive Scientific Advice by EMA**
- **Completion of regulatory prep for MASTERS-2 trial in North America and EU**
- **Launch and first patients enrolled in MASTERS-2 trial**
- **Expansion of contract manufacturing capabilities** to include CMO sites in Japan and Europe
- **Expansion of collaboration with Healios (generating \$43.1 million in initial payments & investment for ATHX)**
- **Maintained healthy balance sheet**
- **Completion of enrollment** for exploratory ARDS trial – and **successful results**
- **Healios initiation of ONE-BRIDGE study for ARDS** and enrollment commenced
- **Fast Track designation for ARDS program**
- **Advancement of other portfolio programs**

► Primary priorities for 2019

- Advancement of TREASURE and MASTERS-2 pivotal trials
- Continued evaluation of additional partnering and collaborative opportunities
- Support of Healios ARDS trial in Japan and completion of 1 year follow up for ARDS clinical trial in U.S. & U.K.
- Continued advancement of key process development and manufacturing initiatives
- Advancement of other portfolio programs